Claims

1. A glycosylated or nonglycosylated proteinaceous compound having agonist activity for at least one glycoprotein hormone

β^1-(linker^1)$_{n^1}$-β^2-(linker^2)$_{n^2}$-β^3-(linker^3)$_{n^3}$-α (1);

β^1-(linker^1)$_{n^1}$-β^2-(linker^2)$_{n^2}$-α-(linker^3)$_{n^3}$-β^3 (2);

β^1-(linker^1)$_{n^1}$-α-(linker^2)$_{n^2}$-β^2-(linker^3)$_{n^3}$-β^3 (3); and

α-(linker^1)$_{n^1}$-β^1-(linker^2)$_{n^2}$-β^2-(linker^3)$_{n^3}$-β^3 (4)

wherein α is the α subunit of a vertebrate glycoprotein hormone or a variant thereof;

each β is independently a glycoprotein β subunit or a variant thereof;

each "linker" is a hydrophilic, flexible spacer equivalent to a peptide containing 1-100 amino acid residues; and

each n is a 0 or 1;

said compound optionally comprising one or more additional β^x(linker^x)$_{n^x}$ and/or one or more additional α subunits.

2. The compound of claim 1 which is of the formula

(1) β^1-(linker^1)$_{n^1}$-β^2-(linker^2)$_{n^2}$-β^3-(linker^3)$_{n^3}$-α ;

(2) β^1-(linker^1)$_{n^1}$-β^2-(linker^2)$_{n^2}$-α-(linker^3)$_{n^3}$-β^3 ;

(3) β^1-(linker^1)$_{n^1}$-α-(linker^2)$_{n^2}$-β^2-(linker^3)$_{n^3}$-β^3 ;

(4) α-(linker^1)$_{n^1}$-β^1-(linker^2)$_{n^2}$-β^2-(linker^3)$_{n^3}$-β^3 ;

(5) β^1(linker^1)$_{n^1}$-β^2(linker^2)$_{n^2}$-β^3(linker^3)$_{n^3}$-β^4(linker^4)$_{n^4}$-α;

(6) β^1(linker^1)$_{n^1}$-β^2(linker^2)$_{n^2}$-β^3(linker^3)$_{n^3}$-α-β^4(linker^4)$_{n^4}$;

(7) β^1(linker^1)$_{n^1}$-β^2(linker^2)$_{n^2}$-α-β^3(linker^3)$_{n^3}$-β^4(linker^4)$_{n^4}$;

(8) β^1(linker^1)$_{n^1}$-α-β^2(linker^2)$_{n^2}$-β^3(linker^3)$_{n^3}$-β^4(linker^4)$_{n^4}$; or

(9) α-β^1(linker^1)$_{n^1}$-β^2(linker^2)$_{n^2}$-β^3(linker^3)$_{n3}$-β^4(linker^4)$_{n^4}$.

3. The compound of claim 1 or 2 wherein each β is different.

4. The compound of claim 1 or 2 wherein at least one linker is independently a complete or partial CTP comprising at least one glycosylation site or a variant thereof, wherein CTP refers to the amino acid sequence at positions 112-118 to 145 of human chorionic gonadotropin β subunit.

5. The compound of claim 1 or 2 which is a protein.

6. The compound of claim 1 or 2 wherein said protein consists of naturally occurring amino acids.

7. The compound of claim 1 or 2 wherein each β and α subunit is human native subunit.

8. The compound of claim 1 which is of formula (1).

9. The compound of claim 8 which is TSHβ-CTP-FSHβ-CTP-CGβ-α.

10. The compound of claim 2 which is of formula (5).

11. The compound of claim 10 wherein each β subunit is different.

12. A pharmaceutical composition which comprises the compound of claim 1 or 2 in admixture with a suitable pharmaceutical excipient.

13. The compound of claim 1 or 2 coupled to a solid support.

14. Antibodies immunospecific for the compound of claim 1 or 2.

15. A DNA or RNA molecule which comprises a nucleotide sequence encoding the protein of claim 6.

16. An expression system for production of an agonist of at least one glycoprotein hormone which expression system comprises a first nucleotide sequence encoding the protein of claim 6 operably linked to control sequences for effecting the expression of said first nucleotide sequence.

17. The expression system of claim 16 which further contains a second nucleotide sequence encoding a signal peptide operably linked to the protein encoded by said first nucleotide sequence.

18. Cells modified to contain the expression system of claim 17.

19. Cells modified to contain the expression system of claim 18.

20. A method to produce a single-chain agonist of at least one glycoprotein hormone which method comprises culturing the cells of claim 18 under conditions wherein said protein is produced; and

recovering said protein from the culture.

21. A method to produce a single-chain agonist of at least one glycoprotein hormone which method comprises culturing the cells of claim 19 under conditions wherein said protein is produced; and

recovering said protein from the culture.